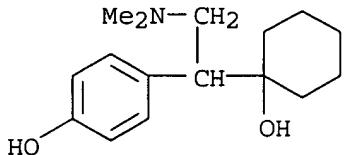


CAS ONLINE PRINTOUT

=> d 11

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 93413-62-8 REGISTRY
ED Entered STN: 18 Dec 1984
CN Phenol, 4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]- (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN 4-[2-(Dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol
CN Desvenlafaxine
CN DVS 233
CN O-Desmethylvenlafaxine
FS 3D CONCORD
DR 130198-07-1
MF C16 H25 N O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOSIS, CA,
CAPLUS, CASREACT, CHEMCATS, HSDB*, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH,
MEDLINE, PHAR, PROMT, PROUSDDR, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

104 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
104 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

CAS ONLINE PRINTOUT

=> d his

(FILE 'HOME' ENTERED AT 08:53:40 ON 01 MAR 2006)

FILE 'REGISTRY' ENTERED AT 08:54:45 ON 01 MAR 2006
E O-DESMETHYLVENLAF/CN

L1 1 S E4

FILE 'CAPLUS' ENTERED AT 08:55:18 ON 01 MAR 2006

L2 104 S L1

L3 0 S L1/PUR

L4 10 S L1/P

=> d bib abs 1-10

L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:759877 CAPLUS

DN 141:277347

TI Improved process for preparation of phenethylamine derivatives, particularly 1-(2-amino-1-phenylethyl)cycloalkanols useful as venlafaxine intermediates, by hydrogenation of corresponding nitriles over cobalt or nickel catalysts at controlled temperatures

IN Kim, Keun-sik; Kim, Kwang-il; Chai, Ki-byung

PA Wyeth, John, and Brother Ltd., USA

SO U.S. Pat. Appl. Publ., 7 pp.

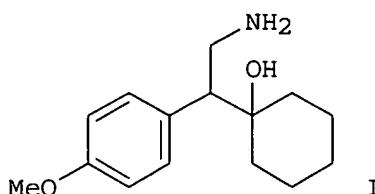
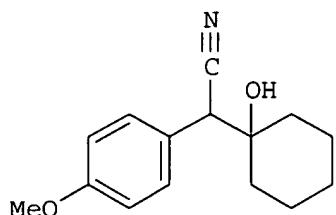
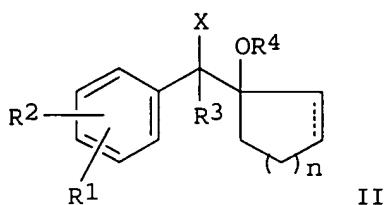
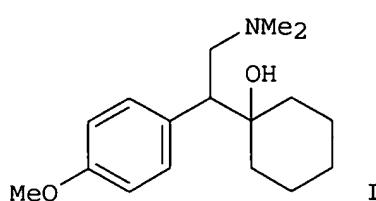
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004181093 CA 2517164 WO 2004080934 WO 2004080934	A1 AA A2 A3	20040916 20040923 20040923 20041028	US 2004-797705 CA 2004-2517164 WO 2004-US7861	20040310 20040309 20040309
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1601640	A2	20051207	EP 2004-718880	20040309
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
	NO 2005004300	A	20050930	NO 2005-4300	20050916
PRAI	US 2003-453583P WO 2004-US7861	P W	20030311 20040309		
OS	CASREACT 141:277347; MARPAT 141:277347				
GI					



AB An improved hydrogenation process for the preparation of certain drug intermediates is disclosed. The process is useful for the preparation of intermediates used in the manufacture of the antidepressant venlafaxine (I) and related compds. Specifically, the claimed process involves preparation of aminomethyl compds. II [X = CH₂NH₂] by hydrogenation of nitriles II [X = cyano] in the presence of a Ni or Co catalyst at a temperature of about 5° to about 25° [wherein: R₁, R₂ = (ortho or para substituents) H, OH, C₁-6 alkyl, C₁-6 alkoxy, C₇-9 aralkoxy, C₂-7 alkanoyloxy, C₁-6 alkylmercapto, halo, or CF₃; R₃ = H or C₁-6 alkyl; R₄ = H, C₁-6 alkyl, formyl, or C₂-7 alkanoyl; n = 0, 1, 2, 3, or 4; dotted line = optional olefinic unsatn.]. The controlled temperature of the process prevents the formation of undesirable phenylalkylamine byproducts, which are typically formed at higher temps., and which are very difficult to sep. Also claimed is a process for alkylation of the obtained primary amines II [X = CH₂NH₂] to give secondary and tertiary amines II [X = NR₅R₆; R₅ = H or C₁-6 alkyl; R₆ = C₁-6 alkyl]. The latter compds. include I and various desmethyl derivs. For example, hydrogenation of nitrile III over Raney Ni in a mixture of MeOH and 25% NH₃ solution, after 20-30 h at room temperature (10-20°) and 60 psi H₂, gave amine IV in 70% yield and 99% purity, directly from the reaction. In contrast, a similar run at higher temps. (25°) gave IV of only 52% purity, with the major impurity (39% of product) being 4-MeOC₆H₄CH₂CH₂NH₂. Alternatively, a too-low temperature run (5°) using more catalyst and NH₃ was still incomplete at 45 h, and also gave IV of only 93% purity.

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:991300 CAPLUS

DN 140:47514

TI Novel formate salt of O-desmethyl-venlafaxine

IN Hadfield, Anthony Francis; Winkley, Michael William

PA Wyeth, John, and Brother Ltd., USA

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003103603	A2	20031218	WO 2003-US18195	20030609
	WO 2003103603	A3	20040325		

CAS ONLINE PRINTOUT

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2488613 AA 20031218 CA 2003-2488613 20030609

US 2003236309 A1 20031225 US 2003-457596 20030609

US 7001920 B2 20060221

BR 2003011693 A 20050322 BR 2003-11693 20030609

EP 1519720 A2 20050406 EP 2003-757455 20030609

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005533772 T2 20051110 JP 2004-510724 20030609

NO 2004005065 A 20050107 NO 2004-5065 20041122

PRAI US 2002-387321P P 20020610

WO 2003-US18195 W 20030609

AB A novel salt of O-desmethylvenlafaxine, O-desmethylvenlafaxine formate, is provided. Pharmaceutical compns., dosage forms and methods of use are also provided.

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:435363 CAPLUS

DN 139:6675

TI Method and solvents for preparing O-desmethylvenlafaxine by the demethylation of venlafaxine with an alkane- or arenethiolate

IN Weber, Beat Theodor

PA Wyeth, John, and Brother Ltd., USA

SO U.S. Pat. Appl. Publ., 3 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003105358	A1	20030605	US 2002-304871	20021126
	US 6689912	B2	20040210		
	CA 2466779	AA	20030612	CA 2002-2466779	20021203
	WO 2003048104	A1	20030612	WO 2002-US38403	20021203
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002357049	A1	20030617	AU 2002-357049	20021203
	BR 2002014701	A	20040831	BR 2002-14701	20021203
	EP 1451143	A1	20040901	EP 2002-804479	20021203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005511681	T2	20050428	JP 2003-549297	20021203
	US 2004158101	A1	20040812	US 2003-750196	20031231
	NO 2004002680	A	20040625	NO 2004-2680	20040625

CAS ONLINE PRINTOUT

PRAI US 2001-334953P P 20011204
 US 2002-304871 A1 20021126
 WO 2002-US38403 W 20021203

OS CASREACT 139:6675

AB O-desmethylvenlafaxine is prepared by reacting venlafaxine with a high-mol.-weight alkane- or arenethiolate anion (e.g., sodium dodecanethiolate) in an alc., ethylene glycol, polyethylene glycol (e.g., PEG 400), ethylene glycol ethers, or their mixts.

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:143294 CAPLUS

DN 136:189323

TI Preparation and pharmaceutical formulation of enantiomers of O-desmethyl venlafaxine

IN Yardley, John P.; Asselin, Andre A.

PA American Home Products Corporation, USA

SO U.S. Pat. Appl. Publ., 8 pp., Cont. of U.S. Ser. No. 590,741, abandoned.
 CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002022662	A1	20020221	US 2001-957908	20010921
	US 2002161055	A1	20021031	US 2002-154994	20020523
	US 2003149112	A1	20030807	US 2003-373145	20030224
	US 2004176468	A1	20040909	US 2004-799321	20040312
	US 2005256206	A1	20051117	US 2005-183573	20050718
PRAI	US 1999-183029P	P	19990615		
	US 2000-590741	B1	20000608		
	US 2001-957908	A1	20010921		
	US 2002-154994	B1	20020523		
	US 2003-373145	A1	20030224		
	US 2004-799321	B1	20040312		

AB This invention provides pharmaceutically active enantiomers of the venlafaxine metabolite O-Desmethyl venlafaxine, R(-)-4-[2-(Dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol or R(-)-1-[2-(dimethylamino)-1-(4-hydroxyphenyl)ethyl]cyclohexanol (I), and S(+)-1-[2-(Dimethylamino)-1-(4-hydroxyphenyl)ethyl]cyclohexanol or S(+)-4-[2-(Dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol, or one or more pharmaceutically acceptable salts or salt hydrates thereof, as well as pharmaceutical compns. utilizing these enantiomers and methods of using the enantiomers to treat, inhibit or control central nervous system disorders. To a solution of 1-[2-(Dimethylamino)-1-(4-methoxyphenyl)ethyl]-cyclohexanol free base (preparation given) in EtOAc at room temperature was added at once to a solution of

(+)-Di-para toluoyl-D-tartaric acid-monohydrate (DT(-)T) and was stirred at room temperature for 1 h. The resulting precipitate was filtered off, washed with

EtOAc, dried overnight at 35° in a vacuum oven to provide crude R(-)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)-ethyl]cyclohexanol DT(-)T salt (yield = 92.8%) as a white solid. The solid was recrystd., and treated with sodium hydroxide solution to obtain I base which was separated and purified. Neurotransmitter uptake inhibition activity of the enantiomers were studied in rats. Pharmaceutical formulations of different enantiomers are disclosed.

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:900601 CAPLUS

DN 134:56475

TI Preparation and formulation of O-desmethyl venlafaxine enantiomers

CAS ONLINE PRINTOUT

IN Yardley, John Patrick; Asselin, Andre Alfred
 PA American Home Products Corporation, USA
 SO PCT Int. Appl., 24 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000076955	A1	20001221	WO 2000-US16388	20000614
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRAI US 1999-183029P P 19990615
 US 1999-333594 A 19990615

AB Title compds. were prepared by optical resolution of venlafaxine followed by O-demethylation. Data for biol. activity of title compds. were given.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2000:384124 CAPLUS
 DN 133:17270
 TI Preparation of (-)-venlafaxine and derivatives as neuronal monoamine reuptake inhibitors.
 IN Jerussi, Thomas P.; Senanayake, Chrisantha H.
 PA Sepracor Inc., USA
 SO PCT Int. Appl., 45 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032556	A1	20000608	WO 1999-US28303	19991201
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US	6342533	B1	20020129	US 1999-450690	19991130
CA	2352324	AA	20000608	CA 1999-2352324	19991201
EP	1135359	A1	20010926	EP 1999-968056	19991201
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP	2003524613	T2	20030819	JP 2000-585198	19991201
AU	774408	B2	20040624	AU 2000-24749	19991201
US	2002086904	A1	20020704	US 2001-14592	20011214
US	6441048	B2	20020827		
US	2003018083	A1	20030123	US 2002-222815	20020819
US	6911479	B2	20050628		
US	2004180952	A1	20040916	US 2004-806423	20040323

CAS ONLINE PRINTOUT

PRAI	US 1998-110488P	P	19981201
	US 1999-450690	A	19991130
	WO 1999-US28303	W	19991201
	US 2001-14592	A3	20011214
	US 2002-222815	A3	20020819

AB A pharmaceutical composition comprising (-)-venlafaxine derivative substantially

free of (+)-stereoisomer is claimed. Thus, (\pm)-venlafaxine in THF was added to a mixture prepared from Ph2PH and BuLi in THF at 0° followed by stirring and overnight reflux to give 73.8% (\pm)-O-desmethylvenlafaxine, which was resolved using di-p-toluoyl-L-tartaric acid to give (-)-O-desmethylvenlafaxine. Drug formulations containing the latter are given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:384122 CAPLUS
DN 133:30575
TI Preparation of derivatives of (+)-venlafaxine as inhibitors of neuronal monoamine reuptake.
IN Jerussi, Thomas P.; Senannayake, Chrisantha H.
PA Sepracor Inc., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032555	A1	20000608	WO 1999-US28306	19991201
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6197828	B1	20010306	US 1999-450691	19991130
	CA 2352321	AA	20000608	CA 1999-2352321	19991201
	EP 1135358	A1	20010926	EP 1999-965065	19991201
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2003501344	T2	20030114	JP 2000-585197	19991201
PRAI	US 1998-110486P	P	19981201		
	US 1999-450691	A	19991130		
	WO 1999-US28306	W	19991201		

AB A method of treating an affective disorder comprises administration of a (+)-venlafaxine derivative substantially free of the (-)-enantiomer. Thus, (\pm)-venlafaxine (preparation given) was added to a 0° mixture of Ph2PH and BuLi followed by stirring and reflux overnight to give 73.8% (\pm)-O-desmethylvenlafaxine, which was resolved to give (+)-O-desmethylvenlafaxine. Drug formulations containing the latter are given.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:81228 CAPLUS

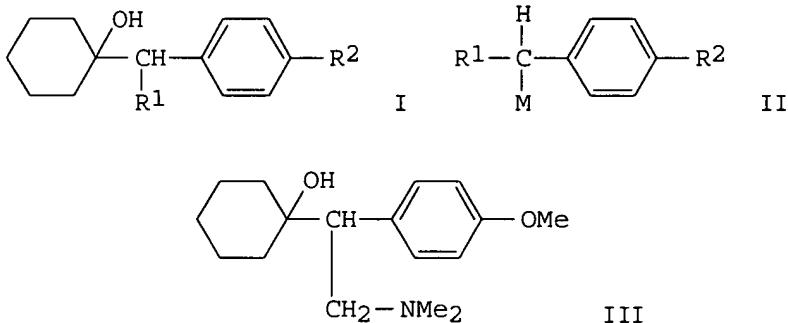
CAS ONLINE PRINTOUT

DN 114:81228
 TI Preparation of cyclohexanol derivatives as intermediates for antidepressants
 IN Shepherd, Robin Gerald
 PA John Wyeth and Brother Ltd., UK
 SO Brit. UK Pat. Appl., 15 pp.
 CODEN: BAXXDU

DT Patent
 LA English

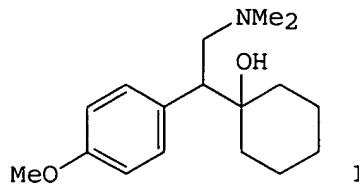
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2227743	A1	19900808	GB 1990-2095	19900130
	GB 2227743	B2	19920617		
	US 5043466	A	19910827	US 1990-471187	19900126
PRAI	GB 1989-2209	A	19890201		
OS	CASREACT 114:81228; MARPAT 114:81228				
GI					



AB Title compds. I [R1 = cyano, CONMe₂, CSNMe₂; R2 = OMe, (protected) OH], useful as intermediates for preparation of antidepressants, were prepared by reaction of II [M = Li, Na, K, or MgX (X = halo); R2 = OMe, protected OH] with cyclohexanone in hydrocarbon/ether solvents. For example, II (R1 = CSNMe₂, R2 = OMe, M = MgBr) gave the corresponding I in 64% yield. Subsequent reduction of I by Raney-Ni gave the antidepressant (no data) N,N-dimethyl-2-(1-hydroxycyclohexyl)-2-(4-methoxyphenyl)ethylamine (III).

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 1990:630878 CAPLUS
 DN 113:230878
 TI 2-Phenyl-2-(1-hydroxycycloalkyl)ethylamine derivatives: synthesis and antidepressant activity
 AU Yardley, John P.; Husbands, G. E. Morris; Stack, Gary; Butch, Jacqueline; Bicksler, James; Moyer, John A.; Muth, Eric A.; Andree, Terrance; Fletcher, Horace, III; et al.
 CS Wyeth-Ayerst Res., Princeton, NJ, 08543-8000, USA
 SO Journal of Medicinal Chemistry (1990), 33(10), 2899-905
 CODEN: JMCMAR; ISSN: 0022-2623
 DT Journal
 LA English
 OS CASREACT 113:230878
 GI



AB A series of 2-phenyl-1-(1-hydroxycycloalkyl)ethylamine derivs. was examined for the ability to inhibit both rat brain imipramine receptor binding and the synaptosomal uptake of norepinephrine (NE) and serotonin (5-HT). Neurotransmitter uptake inhibition was highest for a subset of 2-phenyl-2-(1-hydroxycyclohexyl)dimethylethylamines in which the aryl ring has a halogen or methoxy substituent at the 3- and/or 4-positions. Potential antidepressant activity in this subset was assayed in three rodent models—the antagonism of reserpine-induced hypothermia, the antagonism of histamine-induced ACTH release, and the ability to reduce noradrenergic responsiveness in the rat pineal gland. An acute effect seen in the rat pineal gland with several analogs, including 1-[1-(3,4-dichlorophenyl)-2-(dimethylamino)ethyl]cyclohexanol and 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol (I), was taken as a possible correlate of a rapid onset of antidepressant activity. Compound I (venlafaxine) is presently undergoing clin. evaluation.

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1985:5895 CAPLUS

DN 102:5895

TI Phenethylamine derivatives and intermediates

IN Husbands, George Edward Morris; Yardley, John Patrick; Muth, Eric Anthony

PA American Home Products Corp., USA

SO Eur. Pat. Appl., 58 pp.

CODEN: EPXXDW

DT Patent

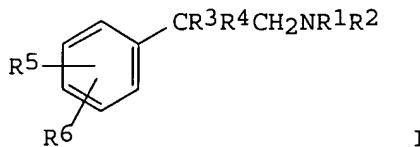
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 112669	A2	19840704	EP 1983-307435	19831207
	EP 112669	A3	19841128		
	EP 112669	B1	19870729		
	R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE				
	US 4535186	A	19850813	US 1983-545701	19831026
	CA 1248540	A1	19890110	CA 1983-441289	19831116
	AU 8322123	A1	19840621	AU 1983-22123	19831206
	AU 567524	B2	19871126		
	ZA 8309073	A	19840926	ZA 1983-9073	19831206
	IL 70390	A1	19861231	IL 1983-70390	19831206
	GB 2133788	A1	19840801	GB 1983-32598	19831207
	GB 2133788	B2	19870715		
	AT 28628	E	19870815	AT 1983-307435	19831207
	FI 8304523	A	19840614	FI 1983-4523	19831209
	FI 77647	B	19881230		
	FI 77647	C	19890410		
	DK 8305713	A	19840614	DK 1983-5713	19831212
	DK 166372	B	19930419		
	DK 166372	C	19930906		
	HU 33097	O	19841029	HU 1983-4231	19831212
	HU 199104	B	19900129		
	ES 527938	A1	19870101	ES 1983-527938	19831212
	JP 59116252	A2	19840705	JP 1983-235979	19831213

CAS ONLINE PRINTOUT

JP 04012260	B4	19920304		
US 4611078	A	19860909	US 1985-736747	19850522
US 4761501	A	19880802	US 1985-736744	19850522
ES 544402	A1	19880401	ES 1985-544402	19850531
GB 2173787	A1	19861022	GB 1986-3901	19860217
GB 2173787	B2	19870715		
JP 03135948	A2	19910610	JP 1990-267502	19901003
JP 04040339	B4	19920702		
JP 03178953	A2	19910802	JP 1990-267501	19901003
JP 05030826	B4	19930511		
PRAI US 1982-449032	A	19821213		
US 1983-486594	A	19830419		
GB 1983-16646	A	19830618		
US 1983-545701	A	19831026		
EP 1983-307435	A	19831207		
GB 1983-32598	A3	19831207		
OS CASREACT 102:5895; MARPAT 102:5895				
GI				



AB About 35 I [R1 = H, C1-6 alkyl; R2 = C1-6 alkyl; R3 = optionally unsatd. 1-hydroxycycloalkyl, optionally unsatd. 1-alkoxycycloalkyl, 1-cycloalkenyl; R4 = H, C1-6 alkyl; R5, R6 = H, OH, C1-6 alkyl, alkoxy, alkanoyloxy, -CN, NO₂, alkylthio, NH₂, alkylamino, dialkylamino, carboxamido, halo, CF₃; R5R6 = methylenedioxy], antidepressants, were prepared E.g., p-MeOC₆H₄CH₂CN in THF was treated with BuLi at -70°, then condensed with cyclohexanone at -50° to give 1-[cyano(p-methoxyphenyl)methyl]cyclohexanol (II). II was hydrogenated in NH₃-EtOH over 5% Rh on Al₂O₃, then methylated with HCHO and HCO₂H to give 1-[(2-dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol (III). III showed an activity equal to imipramine in synaptosomal NE and 5-HT uptake inhibition. Also, unlike the tricyclic antidepressants, III and related compds. demonstrate neither muscarinic anticholinergic activity nor antihistaminic activities.

=> FIL STNGUIDE			
COST IN U.S. DOLLARS		SINCE FILE	TOTAL
		ENTRY	SESSION
FULL ESTIMATED COST		30.73	36.35
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)		SINCE FILE	TOTAL
		ENTRY	SESSION
CA SUBSCRIBER PRICE		-7.50	-7.50

FILE 'STNGUIDE' ENTERED AT 08:57:12 ON 01 MAR 2006
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
 COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Feb 24, 2006 (20060224/UP).

CAS ONLINE PRINTOUT

=>